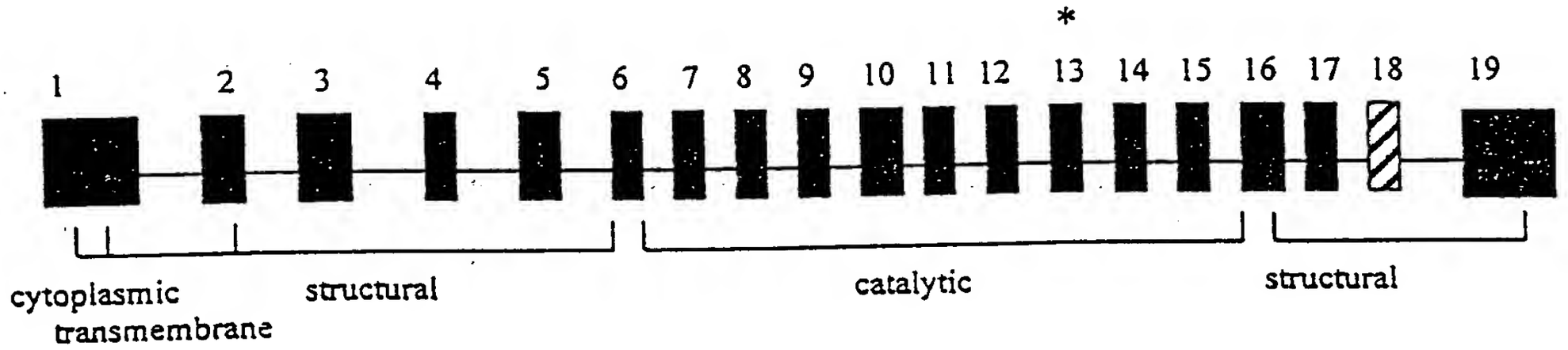
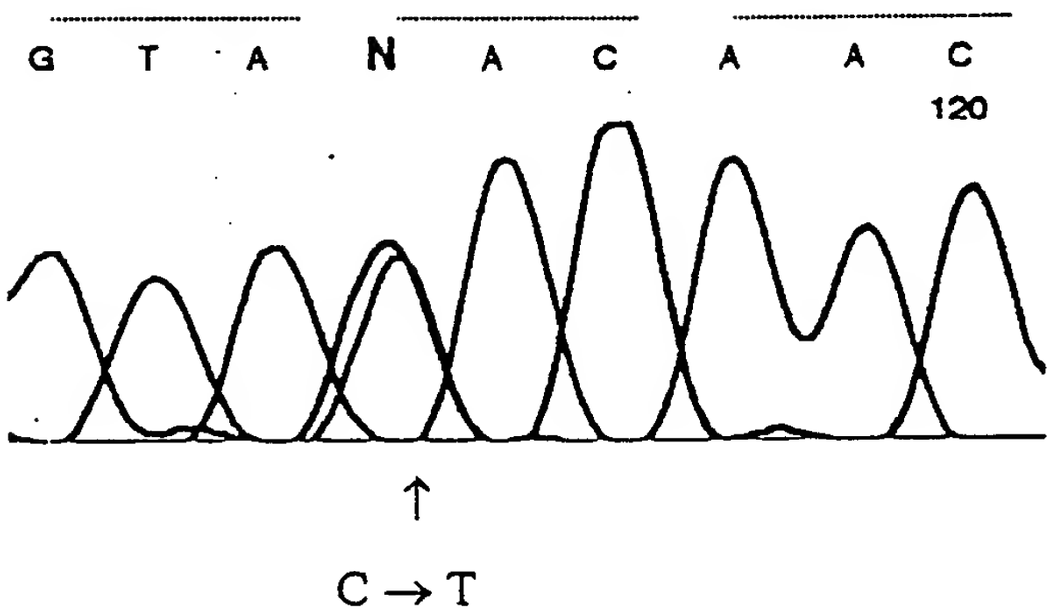


FIG. 1

Proposed exon map of human GCPII based on the genomic sequence of PSMA (O'Keefe, D.S. et al., *Biochim. Biophys. Acta* 1443:113-127 (1998)). The H475Y mutation is localized to exon 13 as shown by *. The exon 18 deletion resulting from the splice variant is shown with hatched bars. The predicted regions coding for the various functional domains are based on the Rawlings and Barrett analysis (Rawlings, N.D. et al., *Biochim. Biophys. Acta* 1139:247-252 (1997)).

a *codon* 474 475 476



mutated

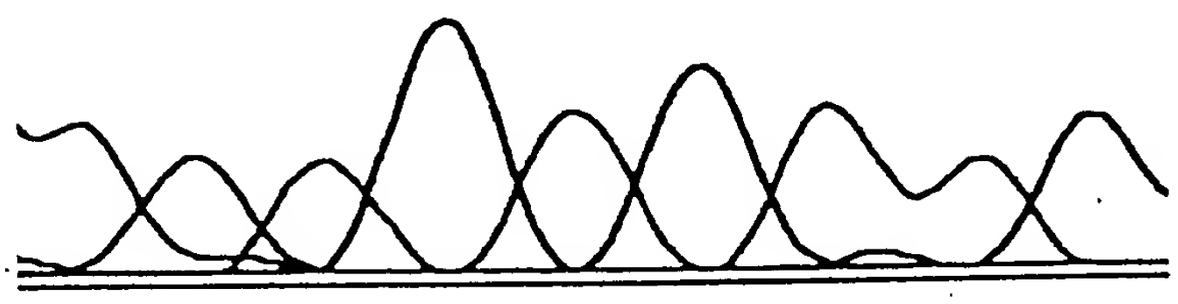
↑

C → T

His → Tyr

b

codon 474 475 476



normal

c

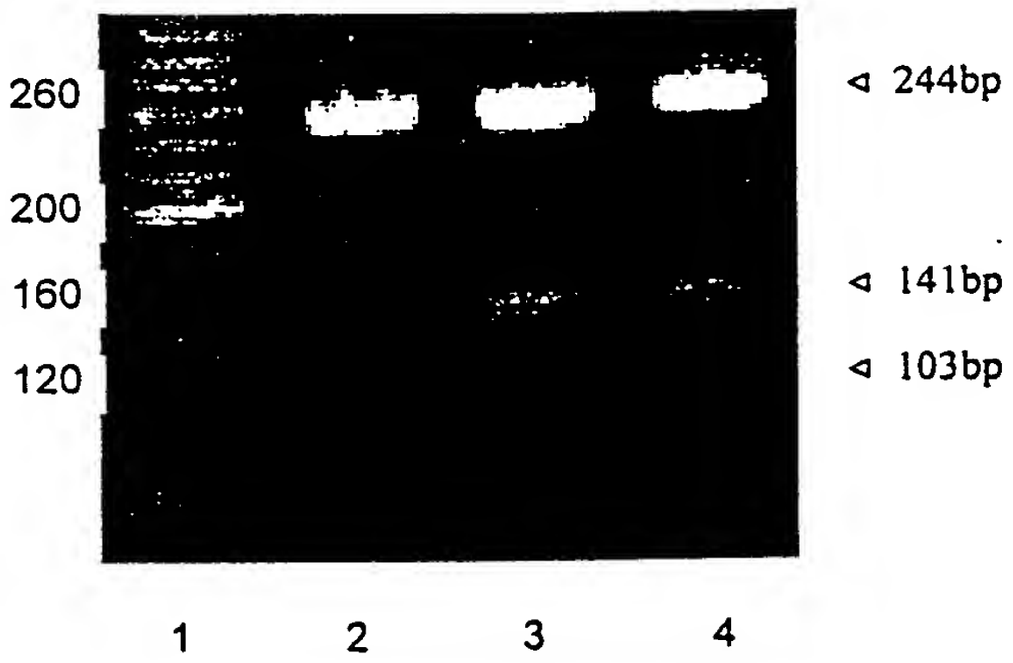
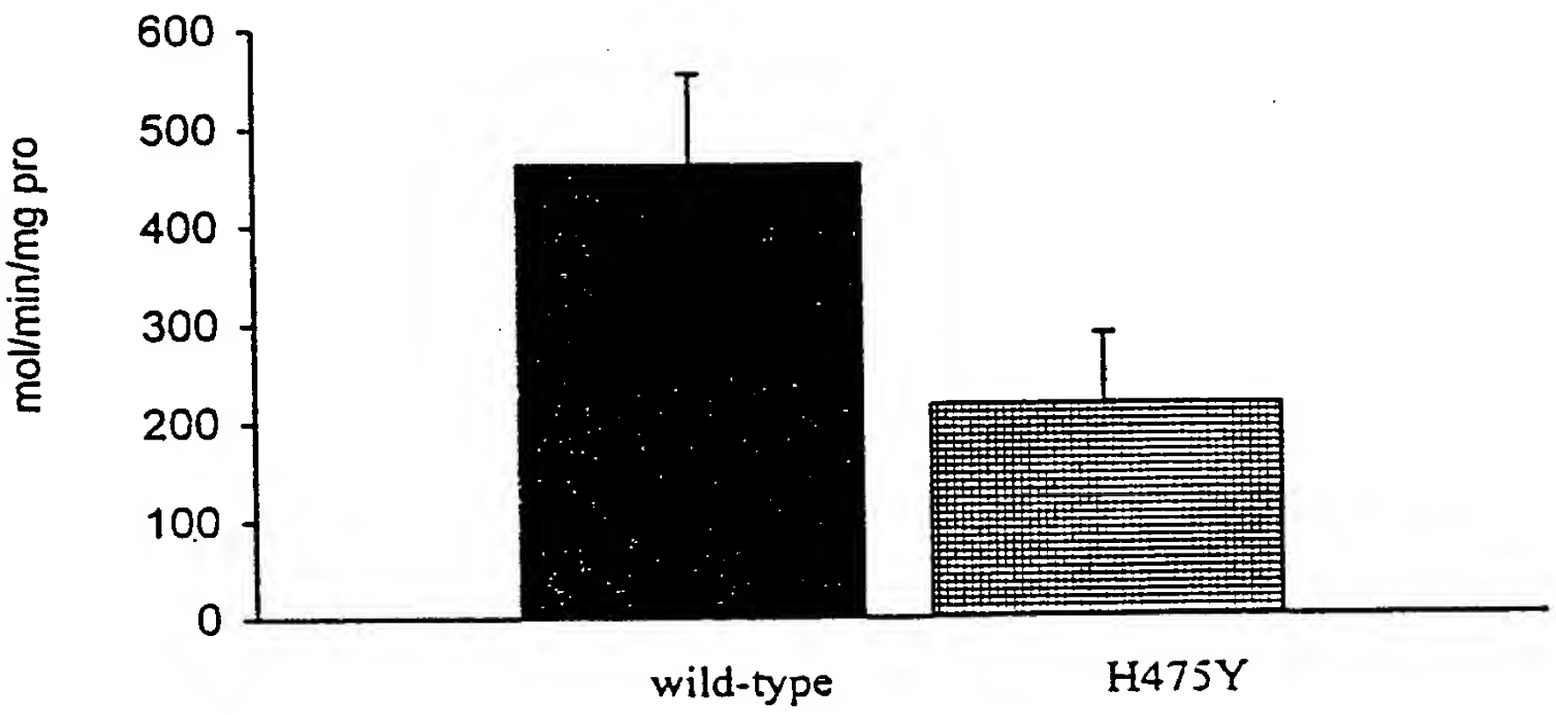


FIG. 2



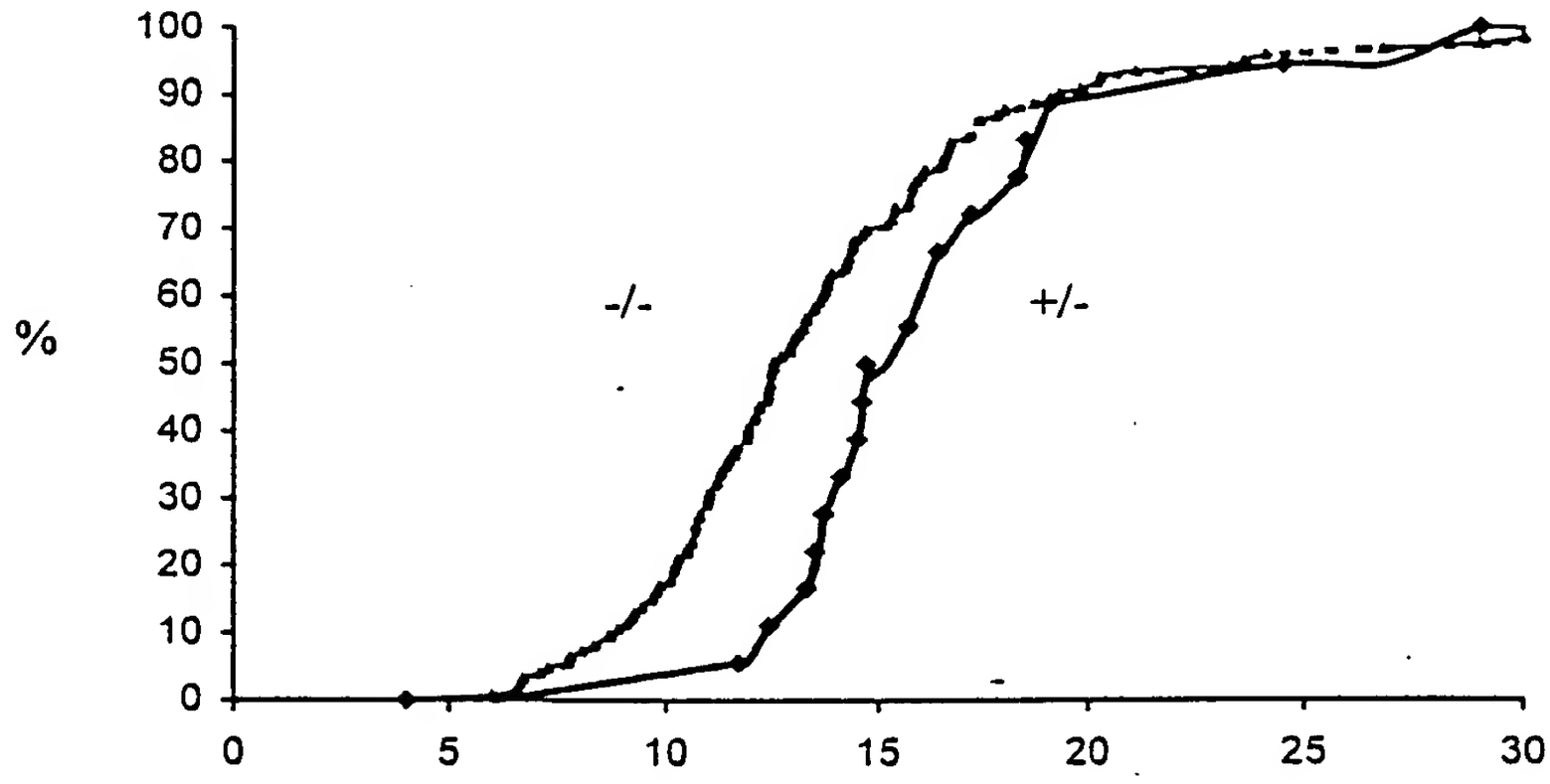
COS-7 Transfectants -
plasmid

FGCP activity in membranes of COS-7 cell transfectants. FGCP activity was determined in membranes from COS-7 cell transfectants using the substrate folyl-γ-glutamyl-γ-[^{14}C]glutamate (Chandler, C.J. et al., J. Biol. Chem. 261:928-933 (1986)); Krumdieck, C.L. et al., Anal. Biochem. 35:123-129 (1970)). COS-7 cells were transfected with constructs of either GCPII cDNA (wild-type) or H475Y mutated GCPII cDNA (H475Y) in pTRACER-CMV2 (Invitrogen). Results show the means+SD of three experiments for each transfectant. There was no activity in mock transfected cells (not shown). FGCP activity was significantly lower ($p<0.01$) in membranes from H475Y mutant transfectants than membranes from wild-type GCPII transfectants.

FIG. 3

a.

b.



. Cumulative frequency distributions of serum folate and homocysteine according to GCPII genotype.

FIG. 4